PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 501717 CJE	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. **PCT/NZ2004/000125**	International filing date *(day/month/year)* 17 June 2004	Priority date *(day/month/year)* 17 June 2003
International Patent Classification (IPC) or national classification and IPC **Int. Cl.** [7] G01N 33/68, C07K 16/18, A61P 19/00		
Applicant PRICKETT, Timothy Charles Ramsey et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. [X] *(sent to the applicant and to the International Bureau)* a total of 3 sheets, as follows:
      [X] sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      [ ] sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. [ ] *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or table related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:

[X]	Box No. I	Basis of the report
[ ]	Box No. II	Priority
[ ]	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
[ ]	Box No. IV	Lack of unity of invention
[X]	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
[ ]	Box No. VI	Certain documents cited
[ ]	Box No. VII	Certain defects in the international application
[ ]	Box No. VIII	Certain observations on the international application

Date of submission of the demand 29 December 2004	Date of completion of the report 10 May 2005
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **ROSS A. OSBORNE** Telephone No. (02) 6283 2404

Form PCT/IPEA/409 (Cover sheet) (January 2004)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/NZ2004/000125

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language which is the language of a translation furnished for the purposes of:

   ☐ international search (under Rules 12.3 and 23.1 (b))

   ☐ publication of the international application (under Rule 12.4)

   ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

   ☐ the international application as originally filed/furnished

   ☒ the description:

   pages **1-41** as originally filed/furnished
   pages* received by this Authority on with the letter of
   pages* received by this Authority on with the letter of

   ☒ the claims:

   pages **42, 44** as originally filed/furnished
   pages* as amended (together with any statement) under Article 19
   pages* **43, 45, 46** received by this Authority on **29/12/2004** with the letter of 20/12/2004
   pages* received by this Authority on with the letter of

   ☒ the drawings:

   pages **1/13 to 13/13** as originally filed/furnished
   pages* received by this Authority on with the letter of
   pages* received by this Authority on with the letter of

   ☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing (*specify*):
   ☐ any table(s) related to the sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing (*specify*):
   ☐ any table(s) related to the sequence listing (*specify*):

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/NZ2004/000125

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-41	YES
	Claims		NO
Inventive step (IS)	Claims	1-41	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-41	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Novelty (N) and Inventive Step (IS)

Claims 1-41 meet the criteria set forth in PCT Articles 33(2) and 33(3) with regard to the requirement for Novelty and Inventive Step. The prior art published before the priority date does not disclose the assessment of skeletal growth using measurements of NT-CNP in a biological sample.

International application No.
PCT/NZ2004/000125

Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material

   [X] a sequence listing

   [ ] table(s) related to the sequence listing

   b. format of material

   [X] in written format

   [ ] in computer readable form

   c. time of filing/furnishing

   [X] contained in the international application as filed

   [ ] filed together with the international application in computer readable form

   [ ] furnished subsequently to this Authority for the purposes of search and/or examination

   [ ] received by this Authority as an amendment* on

2. [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*

10. A method as claimed in claim 9, wherein the binding agent is a monoclonal antibody or monoclonal antibody fragment.

11. A method as claimed in claim 8, wherein the NT-CNP to which the binding agent selectively binds comprises an antigenic peptide selected from the group consisting of proCNP(1-103), proCNP(1-50), proCNP(1-81), and proCNP(51-81).

12. A method as claimed in claim 11, wherein the NT-CNP comprises proCNP(1-50).

13. A method as claimed in any one of claims 8 to 12, wherein binding of NT-CNP is measured using antibodies or antibody fragments that are immobilised to a solid phase.

14. A method for predicting the skeletal growth potential of a subject comprising measuring the level of NT-CNP in a biological sample from said subject, and comparing the level against the mean NT-CNP level of a control population that has attained maximum skeletal growth and predicting from the NT-CNP level in the subject, skeletal growth potential of the subject.

15. A method for predicting the skeletal age of a subject comprising measuring the level of NT-CNP in a biological sample from said subject and comparing the level against the mean NT-CNP level of a control population of known skeletal ages, and predicting from the NT-CNP level in the subject, the skeletal age of the subject.

16. A method for diagnosing a skeletal disease or disorder in a subject comprising measuring the level of NT-CNP in a biological sample from said subject, and comparing the level against the mean NT-CNP level from a control population, wherein a significant deviation in the measured level from the mean control level is indicative of a skeletal disease or disorder.

17. A method as claimed in any one of claims 14 to 16, wherein the biological sample is plasma or whole blood.

18. A method as claimed in any one of claims 14 to 16, wherein subject is a pre-adult.

28. A method as claimed in claim 16, wherein the skeletal disease or disorder is selected from the group comprising congenital disorders, delayed developmental disorders and advanced development syndromes.

29. A method of monitoring skeletal growth in a subject comprising measuring the level of NT-CNP in a first biological sample from the subject and measuring the level of NT-CNP in a second biological sample, wherein the second biological sample is taken from the same subject as the first sample but at a later date, and comparing the levels of NT-CNP in said first and second samples, wherein a significant change in the level of NT-CNP in said second sample from the level of said first sample indicates a change in the rate of skeletal growth.

30. A method as claimed in claim 29, wherein the subject is undergoing a treatment regimen which may impact on skeletal growth of said subject.

31. A method as claimed in any one of claims 6 and 30 ,wherein the treatment regime involves the administration of glucocorticoids to the subject.

32. A method as claimed in claim 31, wherein the subject is undergoing treatment for asthma or other chronic allergic states.

33. A kit for assessing skeletal growth, diagnosing skeletal disease, or predicting skeletal growth potential or skeletal age in a subject comprising means for measuring the level of NT-CNP in a biological sample obtained from said subject, comprising a binding agent that selectively binds to a NT-CNP molecule selected from proCNP (1-103), proCNP(1-50), proCNP (1-81), and proCNP (51-81) and which can be used to quantitatively measure NT-CNP, said kit further comprising instructions for assessing or monitoring skeletal growth, predicting the skeletal growth potential or skeletal age, or diagnosing a skeletal disease or disorder in said subject from the NT-CNP level measured in the biological sample.

34. A kit as claimed in claim 33, wherein the binding agent is selected from the group comprising an anti-NT-CNP antibody, an NT-CNP receptor, or functional fragments or combinations thereof.

35. A kit as claimed in claim 34, wherein the binding agent is a monoclonal antibody or a fragment thereof.

36. A NT-CNP binding agent that selectively binds proCNP (1-50) for use in assessing or monitoring skeletal growth in a subject.

37. A NT-CNP binding agent that selectively binds proCNP (1-50) for use in predicting the skeletal growth potential of a subject, or for predicting the skeletal age in a subject.

38. A NT-CNP binding agent that selectively binds proCNP (1-50) for use in diagnosing a skeletal disease or disorder in a subject.

39. A use of a NT-CNP binding agent in the manufacture of a diagnostic for assessing or monitoring skeletal growth in a subject.

40. A use of a NT-CNP binding agent in the manufacture of a diagnostic for predicting skeletal growth potential or skeletal age in a subject.

41. A use of a NT-CNP binding agent in the manufacture of a diagnostic for diagnosing a skeletal disease or disorder in a subject.